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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/828,815	04/21/2004	Thomas L. Benjamin	00742/062004	7702

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EXAMINER	
LI, QIAN JANICE	
ART UNIT	**PAPER NUMBER**
1633	
MAIL DATE	**DELIVERY MODE**
07/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/828,815	BENJAMIN, THOMAS L.	
	Examiner	Art Unit	
	Q. Janice Li, M.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-8 and 11-23* is/are pending in the application.

4a) Of the above claim(s) *11-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment and response filed 4/9/07 are acknowledged. Claim 1 has been amended. Claims 2, 9, 10 have been canceled. Claims 11-23 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 1, 3-8 are under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated. The arguments in 4/9/07 response would be addressed to the extent that they apply to current rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-8 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Ahlert et al* (Cancer Res 1990;50:5962-8), and as evidenced by *Kroumpouzos et al* (Pigment Cell Res 1994;7:348-53).

Ahlert et al teach a method of generating a virus variant (producing a mutant virus) selectively replicating in human melanoma cells comprising:

(a). providing a wild-type virus Newcastle disease virus strain Ulster (NSV);

(b). introducing random mutations in said virus using UV lamp, thereby obtaining a collection of uncharacterized mutant viruses (column 2, page 5962);

(c). infecting abnormally proliferating cells namely melanoma cells MeWo-M with said collection of mutants for adaptive replication, adapt the virus for growth in said melanoma cells. It is noted the cause of the abnormal proliferation of MeWo is unknown, and MeWo cells do express an oncogene c-myc, and lost the biological active tumor suppressor protein p53 (as evidenced by *Kroumpouzos et al,* e.g. table 1).

(d). selecting a mutant virus NDV1E-10 strain, which is at least 100 times more efficient growing in MeWo melanoma cells compared to the wild type Ulster strain (e.g. the abstract);

(e)-(f). infecting other tumor cells and normal proliferating cells such as mouse and chicken fibroblast and bovine kidney cells (table I), and showing the mutant strain NDV1E-10 was unable to efficiently multiply in 16 of 19 tested cell lines of different tissue and host origin (e.g. 3rd paragraph, column 2, page 5966), and thus a mutant virus with a specific tumor host range was identified.

Ahlert et al go on to teach the selected virus could be used in tumor immune therapy to improve *in vivo* effectiveness of virotherapy of human tumors without significantly increasing the risk of unspecific viral replication in host cells (e.g. the abstract). The teaching of *Ahlert et al* differs from instantly claimed invention in that the illustrated virus is an RNA virus (NDV), thus the starting material is not a wild-type virual DNA. However, given the levels of the skill, it would have been obvious to apply the general method for any type of virus, DNA or RNA. Accordingly, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

In the remarks, the applicant argues that Ahlert fails to teach or suggest using uncharacterized abnormally proliferating cells in a method of producing a virus that is unable to propagate in the uncharacterized abnormally proliferating cells, because the MeWo cells used by Ahlert were characterized.

In response, it is noted that the specification defines "uncharacterized cells" as following (emphasis added):

> "Uncharacterized abnormally proliferating cell," as used herein, refers to a cell where the cause of the abnormal proliferation is unknown. For example, the genetic alteration that results in abnormal proliferation has not been identified. However, other features of the cell may be characterized.

Turn to the *Kroumpouzos* reference, who examined various known oncogene expression in several melanoma cell lines including MeWo cell line, and concluded "THE OBSERVED ONCOGENE EXPRESSION CORRELATED NEITHER WITH GROWTH PARAMETERS NOR MELANIN CONTENT" (see abstract). Accordingly, even though *Kroumpouzos et al* characterized oncogene expression in MeWo cells, they did not find any correlation with the abnormal growth (proliferation), and thus MeWo cells belong to the category "a cell where the cause of the abnormal proliferation is unknown", and thus "uncharacterized. Here, the oncogene expression may be considered as other features of the cell that have been characterized.

On the other hand, the general approach taught by *Ahlert et al* was not limited to any particular cell line such as MeWo cells, but applies to tumor immune therapy in general, and thus any tumor cells, characterized or not. "THIS REPORT SHOWS A PROCEDURE TO GENERATE APATHOGENIC VIRUS VARIANTS SELECTIVELY MULTIPLYING IN TUMOR TISSUE AND

THEREBY MAY OPEN NEW WAYS OF SAFE APPLICATION OF VIRUSES FOR CANCER THERAPY" (last paragraph, page 5967).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method taught by *Ahlert et al,* for generating apathogenic virus variants (T-HR mutant virus) for selective growth in any tumor cells, characterized or not, with a reasonable expectation of success. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is **571-272-0730**. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The **fax** numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is **(866) 217-9197**. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It

also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at **800-786-9199**.

Q. JANICE LI, M.D.
PRIMARY EXAMINER

Q. Janice Li, M.D.
Primary Examiner
Art Unit 1633

QJL
July 5, 2007